

because one of ordinary skill in the art would not have a reasonable expectation of successfully preparing the claimed complex from the cited references, or that it would work for its intended purpose. The Patent Office concedes Ahotupa et al. (Reference A) fails to disclose an inclusion complex of cyclodextrin and HMR (Official Action, page 5, last sentence). Loftsson et al. also fails to disclose or suggest an inclusion complex of a cyclodextrin and HMR, a geometric isomer or stereoisomer thereof, or an HMR ester. Instead, Loftsson et al. is a general review of pharmaceutical uses of cyclodextrin complexes.

When features of prior art references are modified or combined to establish obviousness, the mere possibility of such a combination is insufficient. Instead, references may only be combined when (1) the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or perform the claimed process, and (2) that those of ordinary skill in the art would have a reasonable expectation of success in making the claimed composition or performing the claimed process. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

Loftsson et al. concede that "prediction of compound solubilization by cyclodextrins continues to be highly empirical" (Page 1020, right col., lines 15-16). Indeed, cyclodextrin inclusion complexation is an unpredictable art, both with respect to complex formation and guest molecule stability. See the attached Declaration of Jukka Mönkkönen, which points out that cyclodextrin complexation is complicated and difficult to predict (Paragraph 4.E). Moreover, small structural changes in the guest molecule can have a significant effect on cyclodextrin complexation (Paragraph 4.F). Finally, even if an inclusion complex is formed, it is difficult to predict whether the guest molecule will exhibit increased or decreased stability (Paragraphs 4.G-I).

Dr. Mönkkönen concludes one of ordinary skill in the art would not have a reasonable expectation that a cyclodextrin complex of HMR would be successfully formed from the cited references in view of the unpredictability associated with cyclodextrin inclusion complexation (Paragraph 5). Reconsideration and withdrawal of the obviousness rejection of claims 13-20 over Ahotupa et al. (Reference A) in view of Loftsson et al. are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claims 13-20 over U.S. U.S. Patent Publication 2001/0016590 to Ahotupa et al. (Reference B) in view of Loftsson et al., 85 J. Pharm. Sci. 1017 (1996), is traversed. The claimed inclusion complex comprises a cyclodextrin and hydroxymatairesinol (HMR), a geometric isomer or stereoisomer thereof, or an HMR ester.

Ahotupa et al. (Reference B), like Reference A, also fails to disclose a cyclodextrin inclusion complex of HMR (Official Action, page 9, lines 4-7). Loftsson et al., discussed above, also fails to disclose or suggest an inclusion complex of cyclodextrin and HMR.

The cited combination of references fails to raise a prima facie case of obviousness against the claimed inclusion complex because one of ordinary skill in the art would not have a reasonable expectation of successfully preparing the claimed complex from the cited references. As pointed out in Dr. Mönkkönen's declaration, cyclodextrin complexation is complicated and difficult to predict, with small structural changes in the guest molecule having a significant effect on cyclodextrin complexation. Finally, even if an inclusion complex is formed, it is difficult to predict whether the guest molecule will exhibit

increased or decreased stability. In short, those of ordinary skill in the art would not have a reasonable expectation that a cyclodextrin complex of HMR would be successfully formed from the cited references in view of the unpredictability associated with cyclodextrin inclusion complexation.

Reconsideration and withdrawal of the obviousness rejection of claims 13-20 over Ahotupa et al. (Reference B) in view of Loftsson et al. are respectfully requested.

An Information Disclosure Statement which submits the references cited in Dr. Mönkkönen's declaration is attached.

It is believed this application is in condition for allowance. Reconsideration and withdrawal of all rejections of claims 13-20, and issuance of a Notice of Allowance directed to those claims, are earnestly requested. The Examiner is urged to telephone the undersigned should she believe any further action is required for allowance.

The extension of time and IDS filing fees are being paid electronically today. It is not believed any additional fee is required for entry and consideration of this Amendment.

U.S. Patent Appln. S.N. 10/521,761
REQUEST FOR RECONSIDERATION

PATENT

Nevertheless, the Commissioner is authorized to charge Deposit
Account No. 50-1258 in the amount of any such required fee.

Respectfully submitted,

/James C. Lydon/

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Enclosures:

Petition for Extension of Time
Declaration of Jukka Mönkkönen
Information Disclosure Statement